Complete Summary

GUIDELINE TITLE

European guidelines on cardiovascular disease prevention in clinical practice.

BIBLIOGRAPHIC SOURCE(S)

Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, Dallongeville J, De Backer G, Ebrahim S, Gjelsvik B, Herrmann-Lingen C, Hoes A, Humphries S, Knapton M, Perk J, Priori SG, Pyorala K, Reiner Z, Ruilope L, Sans-Menendez S, Op Reimer WS, Weissberg P, Wood D, Yarnell J, Zamorano JL, Walma E, Fitzgerald T, Cooney MT, Dudina A, Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Funck-Brentano C, Filippatos G, Hellemans I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zamorano JL, Altiner A, Bonora E, Durrington PN, Fagard R, Giampaoli S, Hemingway H, Hakansson J, Kjeldsen SE, Larsen L, Mancia G, Manolis AJ, Orth-Gomer K, Pedersen T, Rayner M, Ryden L, Sammut M, Schneiderman N, Stalenhoef AF, Tokgozoglu L, Wiklund O, Zampelas A, European Society of Cardiology (ESC), European Association for Cardiovascular Prevention and Rehabilitation (EACPR), Council on Cardiovascular Nursing, European Association for Study of Diabetes (EASD), International Diabetes Federation Europe (IDF-Europe), European Stroke Initiative (EUSI), International Society of Behavioural Medicine (ISBM), European Society of Hypertension (ESH), WONCA Europe (European Society of General Practice/Family Medicine), European Heart Network (EHN), European Atherosclerosis Society (EAS). European guidelines on cardiovascular disease prevention in clinical practice: full text. Fourth Joint Task Force of the European Society of Cardiology and other societies [trunc]. Eur J Cardiovasc Prev Rehabil 2007 Sep;14 Suppl 2:S1-113. [1105 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: European guidelines on cardiovascular disease prevention in clinical practice. Eur J Cardiovasc Prev Rehabil 2003 Dec;10(Suppl 1):S1-78.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Cardiovascular disease, including coronary heart disease, stroke, peripheral artery disease and their complications

GUIDELINE CATEGORY

Management
Prevention
Risk Assessment

CLINICAL SPECIALTY

Cardiology
Family Practice
Internal Medicine
Preventive Medicine

INTENDED USERS

Health Care Providers
Physicians

GUIDELINE OBJECTIVE(S)

- To assist physicians and other health professionals to fulfill their role in promoting cardiovascular health and preventing cardiovascular disease, particularly with regard to achieving effective preventive measures in day-to-day clinical practice
- To reflect the consensus arising from a multi-disciplinary partnership between the major European professional bodies represented
- To help health professionals to reduce the occurrence of coronary heart disease, stroke and peripheral artery disease and their complications
- To provide practical and accessible advice with regard to the rationale for prevention, priorities, objectives, risk assessment and management through lifestyle measures and selective drug usage
- To encourage the development of national guidance on cardiovascular disease prevention through the formation of multidisciplinary national guideline and implementation partnerships that are compatible with local political, social, economic and medical circumstances

TARGET POPULATION

- European patients with established atherosclerotic cardiovascular disease (CVD)
- Asymptomatic individuals in Europe who are at increased risk of CVD because of:
    - Multiple risk factors resulting in raised total CVD risk (≥5% 10 year risk of CVD death)
    - Diabetes-type 2 and type 1 with microalbuminuria
    - Markedly increased single risk factors especially if associated with end organ damage
- Close relatives of Europeans with premature atherosclerotic CVD or of those at particularly high risk

INTERVENTIONS AND PRACTICES CONSIDERED

Risk Assessment/Evaluation

1. Risk assessment based on total cardiovascular disease (CVD) risk:
    - History: previous CVD or related diseases, family history of premature CVD, smoking, exercise and dietary habits, social and educational status
    - Examination: blood pressure, heart rate, heart and lung auscultations, foot pulses, body mass index (BMI), waist circumference, fundoscopy in severe hypertension
    - Lab studies: urinary glucose and protein, microalbuminuria, serum cholesterol and if practicable, serum fasting lipids (low-density lipoprotein [LDL] and high-density lipoprotein [HDL] cholesterol, triglycerides), glucose, creatinine, high-sensitivity C-reactive protein, lipoprotein(a), fibrinogen, homocysteine
    - Electrocardiogram (ECG) and exercise ECG
    - Echocardiogram
2. Risk estimation using the Systematic Coronary Risk Evaluation (SCORE) risk prediction system, considering age, gender, smoker status, systolic blood pressure, and cholesterol level
3. New imaging studies to detect asymptomatic individuals at high risk, including carotid artery duplex scanning, electron beam computed tomography (CT), multi-slice CT, ankle/brachial blood pressure ratios, and magnetic resonance imaging (MRI) techniques
4. Consideration of genetic factors (genotypes, phenotypes)
5. Risk assessment in female patients
6. Identification of metabolic syndrome

Management/Prevention

1. Lifestyle interventions
    - Smoking cessation
    - Increased physical activity
    - Weight reduction
    - Reduction in sodium intake
    - Encouraging healthy food choices
    - Reduction in alcohol consumption
2. Anti-hypertensive treatment
    - Diuretics

    - Beta-blockers
    - Angiotensin-converting enzyme (ACE) inhibitors
    - Calcium-channel blockers
    - Angiotensin–receptor blockers (ARBs)
3. Antiplatelet/anticoagulant therapy (aspirin, clopidogrel, warfarin)
4. Anti-hyperlipidemic agents
    - Statins
    - Fibrates
    - Bile acid sequestrants (anion exchange resins)
    - Nicotinic acid and its derivatives
    - Monotherapy versus combination therapy
5. Hypoglycemic drugs for diabetes
6. Establishing treatment targets in patients with type 2 diabetes for glycosylated hemoglobin (HgA_{1c}), plasma glucose, blood pressure, total cholesterol, LDL cholesterol

MAJOR OUTCOMES CONSIDERED

- Cardiovascular disease morbidity and mortality
- Survival rate
- Quality of life
- Risk of myocardial infarction, stroke, and coronary artery disease

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The Task Force has attempted to ensure that the most appropriate evidence is used to underpin recommendations. For population prevention programmes observational epidemiological findings are an important first step in considering causality. Behaviours such as smoking cessation and exercise are less amenable to randomized control trials than drug treatments. Clearly, systematic reviews (http://www.cochrane.org) of observational studies are preferable to citation of single observational studies. For example, individual studies of the relationship between homocysteine and cardiovascular disease have demonstrated variable associations. Pooling data can provide greater understanding of sources of heterogeneity introduced either by study design (e.g., case-control versus cohort) or by the nature of the participants and will provide a more precise estimate of effect. However, it is important to be aware that this increased precision may be spurious if the control for confounding and other biases is weak in the index studies.

A further and growing concern is epidemiology is that with some associations causation has been wrongly attributed. This appears to be the case for antioxidant vitamins where observational studies suggested a reasonable protective effect, but randomized controlled trials have shown that the interventions may even be harmful. Similar concerns have now become apparent with hormone replacement therapy that as thought to confer benefit, but an early systematic review showing adverse cardiovascular effects was ignored until recent randomized controlled trials of hormone replacement therapy confirmed this adverse effect.

A further concern for the Task Force is the nature of available evidence. Much of the evidence concerns drug treatments rather than lifestyle interventions or health system improvements. Since robust evidence from systematic reviews of randomized controlled trials exists for benefits of statins on cardiovascular disease outcomes, the use of such drugs may receive more emphasis that, for example, smoking cessation.

In examining the effects of interventions, the Task Force has given prominence to Cochrane systematic reviews where they exist, as these are conducted to a rigorous standard and are updated periodically. The Task Force has used other systematic reviews where these exist and has only cited individual trials where they make particular points of interest, or are sufficiently large to provide a clear answer to a clinical question. Where the Task Force feels the evidence is scant, they have stated this.

When examining effect sizes the Task Force has not used numbers needed to treat as these have quite marked problems, particularly in preventive cardiology where baseline rates of cardiovascular disease vary markedly throughout Europe. Consequently, a number needed to treat would be needed for countries with low, medium, and high risk. Moreover, numbers needed to treat for different age groups and for men and women would be required. Relative risk reductions of treatment are applicable to all European populations, age groups and men and women as, in general, most treatments have the same relative benefits at different levels of risk.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

These Guidelines attempt to find areas of broad agreement among different professional bodies and scientific disciplines. With the help of the World Organization of National Colleges, Academies and academic associations of general practitioners/family physicians (WONCA) a particular effort has been made to harmonize the advice that may be given to primary care and second-line care health professionals.

The Task Force has attempted to follow an evidence-based approach. They have defined the following questions:

- What is the evidence that specific risk factors cause cardiovascular disease?
- What is the evidence that these risk factors vary in importance among those with and without established cardiovascular disease?
- What is the evidence that interventions for *populations* lead to reductions in risk factors and cardiovascular disease outcomes?
- What is the evidence that interventions for individuals lead to reductions in risk factors and cardiovascular disease outcomes?

The Task Force has systematically and critically reviewed the relevant literature to answer each question posed.

Difficulties with regard to the current European Society of Cardiology (ESC) hierarchical grading system were raised. The present system is likely to favour drug treatments over major lifestyle measures because the latter are less amenable to double blind randomized control trials. For this reason, after prolonged debate, the Task Force has not included tables of the grades that it prepared. However, it is anticipated that this issue will require further debate.

In formulating these updated guidelines on cardiovascular disease (CVD) prevention, The Fourth Joint Task Force has taken note of feedback in several areas:

1. The guidelines are becoming long and unwieldy. Contributors were asked to summarize key points from the Third Joint Task Force Guidelines, but to focus on what is new. The full text of the Guidelines remains available on www.escardio.org.
2. More detailed guidance was sought from the World Organization of National Colleges, Academies and academic associations of general practitioners/family physicians (WONCA) and from the European Society of Cardiology (ESC) Working Group on Cardiovascular Nursing, since these bodies represent the professionals that are heavily engaged in the practical delivery of preventive advice in many European countries.
3. The Systematic Coronary Risk Estimation (SCORE) risk charts may overestimate risk in countries that have experienced a decline in CVD mortality, and underestimate risk if mortality has increased. The development of national guidance has always been recommended by the Task Force and, as part of this process, recalibration of the SCORE charts to allow for time

trends in both mortality and risk factor distributions is recommended. In the third Joint Guidelines the need to address the problem of a high relative but low absolute risk in younger persons was dealt with by extrapolating a young person's risk to age 60 to flag persons who will become at high absolute risk. If interpreted too literally, this approach might result in excessive use of drug treatments in young people. In the present guidelines, this approach has been replaced with a simple relative risk chart to be used in conjunction with the SCORE absolute risk chart.

4. A re-examination of the SCORE data sets indicated that the impact of self-reported diabetes on risk may leave been underestimated. The issue of predicting total events as well as just CVD mortality also receives more attention.
5. A separate section on gender issues has been added.
6. Renal impairment may have been underestimated as a risk factor and is dealt with in more detail.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Published cost analyses were reviewed.

- The estimated total costs of cardiovascular diseases in the European Union countries were 168,767 million Euro in 2003.
- Coronary heart disease secondary prevention programs have proven to be effective in improving processes of care, readmissions to hospital, functional status and overall mortality, especially if they incorporate exercise programs. However, the effect sizes are quite modest and their cost effectiveness on a large scale remains uncertain.
- There is no evidence that mass screening for detection of early stages of coronary heart disease or stroke is a cost-effective way to prevent disease.
- Current data support the implementation of cascade testing for familial hypercholesterolaemia (FH) as being feasible and cost-effective but national implementation is limited to a small number of countries. Funding and the infrastructure to support it may be the major stumbling blocks in implementing this in many countries.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A list of guideline document reviewers, who are independent of the Task Force, is provided in the original guideline document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Priorities, Total Risk Estimation and Objectives

What Are the Priorities for Cardiovascular Disease (CVD) Prevention in Clinical Practice?

1. Patients with established atherosclerotic CVD
2. Asymptomatic individuals who are at increased risk of CVD because of:
    - Multiple risk factors resulting in raised total CVD risk (≥5% 10 year risk of CVD death)
    - Diabetes-type 2 and type 1 with microalbuminuria
    - Markedly increased single risk factors especially if associated with end organ damage
3. Close relatives of subjects with premature atherosclerotic CVD or of those at particularly high risk

What Are the Objectives of CVD Prevention?

1. To assist those at low risk of CVD to maintain this state lifelong, and to help those at increased total CVD risk to reduce it
2. To achieve the characteristics of people who tend to stay healthy:
    - No smoking
    - Healthy food choices
    - Physical activity: 30 min of moderate activity a day
    - Body mass index (BMI) <25 kg/m^2 and avoidance of central obesity
    - Blood pressure (BP) <140/90 mmHg
    - Total cholesterol <5 mmol/l (~190 mg/dl)
    - Low-density lipoprotein (LDL) cholesterol <3 mmol/l (~115 mg/dl)
    - Blood glucose <6 mmol/l (~110 mg/dl)
3. To achieve more rigorous risk factor control in high risk subjects, especially those with established CVD or diabetes:
    - Blood pressure under 130/80 mmHg if feasible
    - Total cholesterol <4.5 mmol/l (~175 mg/dl) with an option of <4 mmol/l (~155 mg/dl) if feasible
    - LDL cholesterol <2.5 mmol/l (~100 mg/dl) with an option of <2 mmol/l (~80 mg/dl) if feasible
    - Fasting blood glucose <6 mmol/l (~110 mg/dl) and glycosylated haemoglobin (HbA1c) <6.5% if feasible
4. To consider cardioprotective drug therapy in these high risk subjects, especially those with established atherosclerotic CVD

When Do I Assess Cardiovascular Risk?

1. If the patient asks for it
2. If, during a consultation:
    - The person is a middle aged smoker
    - There is obesity, especially abdominal
    - One or more risk factors such as blood pressure, lipids or glucose is raised
    - There is a family history of premature CVD or of other risk factors
    - There are symptoms suggestive of CVD. If confirmed, risk factors should be assessed but use of the Systematic Coronary Risk Evaluation (SCORE) chart is not necessary as the person is already at high risk.

Why Stress Assessment of Total CVD Risk?

1. Multiple risk factors usually contribute to the atherosclerosis that causes CVD.
2. These risk factors interact sometimes multiplicatively.
3. Thus the aim should be to reduce total risk; if a target cannot be reached with one risk factor, total risk can still be reduced by trying harder with others.

How Do I Assess CVD Risk Quickly and Easily?

1. Those with:
    - Known CVD
    - Type 2 diabetes or type 1 diabetes with microalbuminuria
    - Very high levels of individual risk factors are already at INCREASED CVD RISK and need management of all risk factors
2. For all other people, the SCORE risk charts can be used to estimate total risk—this is critically important because many people have mildly raised levels of several risk factors that, in combination, can result in unexpectedly high levels of total CVD risk.

Assessing Cardiovascular Risk: What Are the Components?

1. History: Previous CVD or related diseases, family history of premature CVD, smoking, exercise and dietary habits, social and educational status.
2. Examination: BP, heart rate, heart and lung auscultations, foot pulses, height, weight, BMI, waist circumference. Fundoscopy in severe hypertension.
3. Lab test: Urine for glucose and protein, microalbuminuria in diabetics. Cholesterol and if practicable, fasting lipids (LDL- and high-density lipoprotein

[HDL]-cholesterol, triglycerides) glucose, creatinine.
4. Electrocardiogram (ECG) and exercise ECG if angina suspected.
5. ECG and consider echocardiogram in hypertensive persons.
6. Premature or aggressive CVD especially with a family history of premature CVD: consider high sensitivity C-reactive protein (CRP), lipoprotein (a), fibrinogen, homocysteine if feasible, specialist referral.

How Do I Use the SCORE Charts to Assess Total CVD Risk in Asymptomatic Persons?

1. Use the low risk chart in Belgium*, France, Greece*, Italy, Luxembourg, Spain*, Switzerland and Portugal; use the high risk chart in other countries of Europe.

   *Updated, recalibrated charts are now available for Belgium, Germany, Greece, the Netherlands, Poland, Spain and Sweden.

2. Find the cell nearest to the person's age, cholesterol and BP values, bearing in mind that risk will be higher as the person approaches the next age, cholesterol or BP category.
3. Check the qualifiers.
4. Establish the absolute 10 year risk for fatal CVD. Note that a low absolute risk in a young person may conceal a high relative risk; this may be explained to the person by using the relative risk chart. As the person ages, a high relative risk will translate in to a high absolute risk. More intensive lifestyle advice will be needed in such persons.

Risk Estimation Using SCORE: Qualifiers

1. The charts should be used in the light of the clinician's knowledge and judgement, especially with regard to local conditions.
2. As with all risk estimation systems, risk will be overestimated in countries with falling CVD mortality rate, and underestimated if it is rising.
3. At any given age, risk appears lower for women than men. This is misleading since, ultimately, more women than men die from CVD. Inspection of the charts shows that their risk is merely differed by 10 years.
4. Risk may be higher than indicated in the chart in:
   - Sedentary or obese subjects, especially those with central obesity
   - Those with a strong family history of premature CVD
   - The socially deprived
   - Subjects with diabetes – risk may be 5 fold higher in women with diabetes and 3 fold higher in men with diabetes compared to those without diabetes
   - Those with low HDL cholesterol or high triglycerides
   - Asymptomatic subjects with evidence of preclinical atherosclerosis, for

example, a reduced ankle-brachial index or on imaging such as carotid ultrasonography or computed tomography (CT) scanning

How Do I Manage the Components of Total CVD Risk?

1. The patient and the doctor agree that a risk assessment is indicated, and the patient is informed that the result may lead to suggestions regarding lifestyle change and the possibility of lifelong medication.
2. There are time and resources to discuss and follow up advice and treatment.
3. The doctor should be aware of and respect the patient's own values and choices.

Total CVD Risk Management: A Key Message

1. Management of the individual components of risk such as smoking, diet, exercise, blood pressure and lipids impacts on total risk.
2. Thus, if perfect control of a risk factor is difficult (for example, blood pressure control in the elderly), total CVD risk can still be reduced by reducing other risk factors such as smoking or blood cholesterol.

Principles of Behaviour Change and Management of Behavioural Risk Factors

Managing Total CVD Risk - Tips to Help Behaviour Change

1. Develop a sympathetic alliance with the patient
2. Ensure the patient understands the relationship between lifestyle and disease
3. Use this to gain commitment to lifestyle change
4. Involve the patient in identifying the risk factors to change
5. Explore potential barriers to change
6. Help design a lifestyle change plan
7. Be realistic and encouraging—'ANY increase in exercise is good and can be built on'
8. Reinforce the patient's efforts to change
9. Monitor progress through follow-up contacts
10. Involve other healthcare staff wherever possible

Managing Total CVD Risk - Why Do People Find It Hard to Change Their Lifestyle?

1. Socioeconomic status (SES): Low SES, including low educational level and low income, impedes the ability to adopt lifestyle change.
2. Social isolation: People living alone are more likely to have unhealthy lifestyles.
3. Stress: Stress at work and at home makes it more difficult for people to adopt and sustain a healthy lifestyle.
4. Negative emotions: Depression, anxiety and hostility impede lifestyle change.
5. Complex or confusing advice.

Increased physician awareness of these factors facilitates empathy, counselling and the provision of sympathetic, simple and explicit advice.

Recommendations for Good and Effective Physician/Caregiver-Patient Interactions

- Spend enough time with the patient; even 2 min more can make a difference
- Listen carefully to the patient and recognize strengths and weaknesses in the patient's attitude to illness and lifestyle change
- Accept the patient's personal view of his/her disease and allow expression of worries and anxieties
- Speak to the patient in his/her own language and be supportive of every improvement in lifestyle
- Make sure that the patient has understood your advice and has the means to follow it
- Acknowledge that changing life-long habits can be difficult and that gradual change that is sustained is often more permanent
- Be prepared that your patient may need your support for a long time and that repeated efforts to encourage and maintain lifestyle change may become necessary in many patients

Ten Strategic Recommendations to Enhance the Effectiveness of Behavioural Counselling

- Develop a therapeutic alliance
- Counsel all patients
- Ensure that patients understand the relationship between behaviour and health
- Help patients to assess the barriers to behaviour change
- Gain commitments from patients to behaviour change
- Involve patients in identifying and selecting the risk factors to change
- Use a combination of strategies including reinforcement of patient's own capacity for change
- Design a lifestyle modification plan
- Monitor progress through follow-up contact
- Involve other healthcare staff wherever possible

Recommendations to Add Psychosocial Interventions

- In patients with manifest CVD or very high risk, add psychosocial and/or psychoeducational components to standard cardiological care in order to improve risk factor control and quality of life
- Individualize intervention programs to patients' individual risk profiles, age, socioeconomic status and gender

Smoking

Managing Total CVD Risk - Smoking

All smokers should be professionally encouraged to permanently stop smoking all forms of tobacco. The five A's can help:

A –ASK: Systematically identify all smokers at every opportunity
A –ASSESS: Determine the person's degree of addiction and his/her readiness to cease smoking
A –ADVISE: Unequivocally urge all smokers to quit
A –ASSIST: Agree on a smoking cessation strategy including behavioural counselling, nicotine replacement therapy and/or pharmacological intervention
A –ARRANGE a schedule of follow-up visits

Smoking and Risk of CVD

- Smoking of tobacco is a strong and independent risk factor for CVD in asymptomatic patients and in patients with CVD.
- Passive smoking is also associated with an increase in CVD risk.
- The effects of smoking on CVD interact synergistically in the presence of other CVD risk factors.

Nutrition, Overweight and Obesity

Managing Total CVD Risk - Healthy Food Choices

All individuals should be advised about food choices that are associated with a lower CVD risk. High risk persons should receive specialist dietary advice if feasible.

General recommendations should suit the local culture:

1. A wide variety of foods should be eaten.
2. Energy intake should be adjusted to avoid overweight.
3. Encourage: Fruits, vegetables, wholegrain cereals and bread, fish (especially oily), lean meat, low fat dairy products.
4. Replace saturated fats with the above foods and with monounsaturated and polyunsaturated fats from vegetable and marine sources to reduce total fat to <30% of energy, of which less than 1/3 is saturated.
5. Reduce salt intake if blood pressure is raised by avoiding table salt and salt in cooking, and by choosing fresh or frozen unsalted foods. Many processed and prepared foods, including bread, are high in salt.

Managing Total CVD Risk - Body Weight

1. Increasing body weight is associated with increased total and CVD mortality and morbidity, mediated in part through increases in blood pressure and blood cholesterol, reduced HDL cholesterol and an increased likelihood of diabetes.
2. Weight reduction is recommended in obese people (BMI ≥30 kg/m^2) and should be considered for those who are overweight (BMI ≥25 and <30 kg/m^2).
3. Men with a waist circumference of 94 to 102 cm and women with a waist circumference of 80 to 88 cm are advised not to increase their weight. Men above 102 cm and women above 88 cm are advised to lose weight.
4. Restriction of total calorie intake and regular physical exercise are the cornerstones of weight control. It is likely that improvements in central fat metabolism occur with exercise even before weight reduction occurs.

Management

Nutritional Treatment of Cardiovascular Diseases

- Nutrition is an integral part of cardiovascular patient treatment. All patients with cardiovascular disease and individuals at high risk should be given recommendations on the food and dietary options which reduce the cardiovascular risk.
- Dietetic recommendations should be defined individually, taking into account the individual's risk factors – dyslipidaemia, hypertension, diabetes and obesity.
- Within the family setting, the role of the person in charge of buying and cooking food is clearly important.

General Recommendations

- Eating food from each major food group will ensure the appropriate supply of nutrients, minerals and vitamins.
- The intake of fish, fruit and vegetables, cereals and whole grain products, skimmed dairy products, low salt and lean meat is encouraged.
- Energy intake should be adjusted to maintain ideal weight.
- Eating oily fish and omega-3 fatty acids (FAs) may be associated with a reduction in risk of fatal cardiovascular accidents.
- Replacement of saturated and *trans* FAs with monounsaturated or polyunsaturated fats of vegetable origins decreases LDL-cholesterol.
- Eating fruit and vegetables and restricting salt is associated with lower blood pressure.

Specific Recommendations

LDL-Cholesterol

A reduction in plasma LDL-cholesterol is obtained by:

- Lowering the intake of saturated FAs and *trans* FAs and, to a lesser extent, by reducing the intake of cholesterol in food. Saturated and *trans* FA should be substituted for polyunsaturated fat of vegetal origin.
- Saturated fats are found in a wide variety of foods including meat and dairy products, meat pies, sausages, cheese, butter and lard, pastry, cakes, biscuits, cream, coconut oil, palm oil and in a large number of processed foods.
- *Trans* FAs are found in animal-based foods. Dairy and beef fat typically contains around 3 to 6% TFAs (% of total fatty acids). The TFA content of bakery products (rusks, crackers, biscuits, etc.) as well as some breakfast cereals with added fat, French fries, soup powders and some sweet snack products and hard margarine may vary considerably (from below 1% up to 30%). Soft margarines contain only trace TFAs. Consumers are invited to check saturated and *trans* FA content on food labels.
- Soluble fibres and phytosterols may help to reduce the plasma concentrations of LDL-cholesterol.

HDL-Cholesterol

An increase in the concentration of plasma HDL-cholesterol is obtained by:

- Increasing exercise in sedentary individuals, weight loss in obese individuals and controlling glycaemia in diabetic individuals.
- Eating refined sugars is associated with a reduction in HDL-cholesterol concentrations among certain susceptible individuals. These sugars should be replaced with complex sugars.
- Olive oil may help to increase HDL-cholesterol levels. An increase in monounsaturated FA may be recommended in patients with the metabolic syndrome.
- The moderate use of alcohol may increase HDL-cholesterol. While not a positive recommendation, it is not contraindicated in individuals with a low HDL-cholesterol concentration.

Triglycerides

Lowering triglycerides is obtained by:

- Increasing exercise in sedentary patients, weight loss for obese patients and controlling glycaemia for diabetic patients.
- The intake of refined sugars and alcohol should be controlled as it is associated with increases in plasma triglycerides, among certain susceptible patients.
- The intake of omega-3 FAs present in oily fish and some vegetable oils can contribute to a decrease in plasma triglyceride concentrations.

Arterial Blood Pressure

Lowering blood pressure is obtained by:

- Weight loss for overweight/obese patients, controlling the intake of salt and alcohol and increasing the intake of potassium.

- To reduce salt intake, consumers should choose fresh or frozen foods low in salt and limit the amount of salt added to food. Because the vast majority of ingested salt comes from processed foods, any meaningful strategy to reduce salt intake must involve food manufacturers. Consumers are invited to check food labels for salt content.
- Fruit and vegetables should be preferred as a source of potassium rather than supplements.

Practice Points

- Overweight people are at increased risk of diabetes, hypertension, and dyslipidaemia and of many causes of general and cardiovascular illness and death.
- Overweight with consequent adverse effects on cardiovascular risk such as diabetes is increasing in all developing and developed countries.
- Intra-abdominal fat is metabolically active and more strongly associated with risk than total body weight.
- The most widely accepted measures of overweight are BMI and waist circumference (WC). WC may be a slightly better estimator of CVD risk but may be more prone to measurement error.
- WC of 80 cm in women and 94 cm in men represents the level at which no further weight should be gained and WC of 88 cm in women and 102 cm in men represents the level at which weight reduction should be advised.
- Effective weight reduction, especially when combined with exercise reduces cardiovascular risk factor levels.
- It is not yet certain that weight reduction alone reduces mortality.
- It is not known whether drug treatment of overweight has the same, less or more impact on cardiovascular risk as lifestyle change.

Physical Activity

Managing Total CVD Risk - Physical Activity

1. Stress that the positive health benefits occur with almost any increase in activity; small amounts of exercise have an additive effect; exercise opportunities exist in the workplace, for example, by using stairs instead of the lift.
2. Try to find leisure activities that are positively enjoyable.
3. 30 minutes of moderately vigorous exercise on most days of the week will reduce risk and increase fitness.
4. Exercising with family or friends tends to improve motivation.
5. Added benefits include a sense of well being, weight reduction and better self esteem.
6. Continued physician encouragement and support may help in the long-term.

Practice Point: A lack of regular physical activity may contribute to the early onset and progression of cardiovascular disease. Assessment of physical activity should be an integral part of risk evaluation and facilitation of leisure exercise is an important

part of preventive public health efforts.

Health benefits occur with almost any increase in physical activity at any age; this is an important and powerful message to help people to start to become more active.

Estimating Physical Activity

For an assessment of physical active three different methods may be used: (i) criterion methods, for example, doubly labelled water, indirect calorimetry or direct observation, (ii) objective methods, for example, activity monitors (pedometers, accelerometers) or heart rate monitors, (iii) subjective methods such as questionnaires or activity diaries. For physical fitness and exercise capacity maximal incremental exercise testing is used.

Assessment in Children and Adolescents

The assessment of physical fitness in the general population of young people remains the responsibility of school health facilities and primary care physicians. Accurate assessment is necessary to identify current levels of activity and to demonstrate the effectiveness of programmes provided to increase physical activity.

In high-risk individuals for example children with hereditary dyslipidemia or with a high CVD burden in the family and children suffering from diabetes mellitus, a formal assessment using standard exercise testing may be used in order to provide a starting point for lifestyle counselling.

Assessment in Adults without CVD

In the prevention of CVD in the clinical practice the assessment of physical activity and fitness should be combined with a total risk assessment according to the SCORE/HeartScore method.

In low-risk individuals (<5% CVD mortality within 10 years and without previous CVD, diabetes mellitus or markedly elevated single risk factors), a brief interview concerning the person's physical activity at work and leisure gives the basis for assessing his or her general level of fitness and the need to give advice for an increase in physical exercise. There are several self-reported recall questionnaires available. Even diaries for noting daily physical activity may be useful.

In high-risk persons (≥5% CVD 10-year mortality risk at present age or extrapolated to the age of 60, diabetes mellitus or markedly elevated blood pressure and/or blood lipid levels) this may be completed with an exercise test using a bicycle ergometer or treadmill for diagnostic purposes and in order to obtain an objective estimate of the exercise capacity of the individual.

Assessment in Adults with CVD

The medical and social history of CVD patients usually needs supplementary objective assessment using exercise testing procedures in order to detect myocardial ischaemia, to stratify for risk of a further major ischaemic event, to

select for coronary arteriography and to assess the impact of revascularization or the response to antianginal medication.

Assessment in the Elderly

As in the younger age groups the patient interview remains the basis for assessing physical activity. In the elderly the specific problems of deteriorating physical capacity, especially regarding the activities of daily living and the need of social support, should be addressed.

Exercise testing on a bicycle ergometer or treadmill may be needed in persons with symptoms of CVD. Less resource demanding methods as the 6-min Walk Test or the Shuttle Walk Test may also provide valuable information of the physical capacity of the elderly. Recommendations for physical activity are summarized in the table below.

Table: Recommendations for Physical Activities

Aim

- In all age groups: 30-45 min of physical activity at least five days a week

Rationale

- To prevent or delay the onset of cardiovascular disease
- To limit the progress of cardiovascular disease

Method

- Promote daily physical activity at school
- Provide options for regular physical activity at the work site, encourage an active leisure time, e.g., brisk walking, cycling, swimming, gardening or other in/outdoor sports and hobbies
- For coronary patients: participation in supervised or home-based programmes of physical training
- For elderly: stimulate the maintenance of a physically active lifestyle, even in higher age groups

Results

- Lower risk of cardiac mortality and morbidity
- Adequate level of physical fitness, increase of VO_2 max (measure of oxygen uptake) and endurance capacity
- Lowering of heart rate and blood pressure
- Improvement of coronary blood flow
- Effect on symptoms of angina pectoris
- Adaptation of the peripheral resistance
- Protective effect on the sympatico-vagal balance
- Reduction of overweight
- Cardioprotective effect on lipid metabolism and insulin sensitivity

- Effect on platelets and fibrinolysis

Management of Physical Activity

Practice Point: All individuals should be professionally encouraged and supported to increase their physical activity to the level associated with the lowest risk of CVD. Although the goal is at least half an hour of physical activity on most days of the week, almost any increase in activity is associated with a variety of health benefits – a very encouraging message.

Healthy people should be recommended to choose enjoyable activities which fit into their daily routine preferably for 30 to 45 min, 4 to 5 times weekly at a 60 to 75% of the age-adapted maximum heart rate. For patients with established CVD and for those with a high CVD 10-year mortality risk, advice must be based on a comprehensive clinical judgement, including the results of an exercise test.

In addition to improving aerobic fitness, physical activities that facilitate endurance strength balance and flexibility should be encouraged.

Recommendations Concerning Heart Rate in Risk Estimation Systems

Given the lack of randomized controlled trials investigating whether heart rate reduction in the healthy population is beneficial in terms of primary prevention of CVD, it would not be reasonable to recommend pharmacological reduction of heart rate in asymptomatic people with elevated resting heart rate at this time. However, prevention of elevated resting heart rate through lifestyle measures such as regular physical activity, and avoidance of psychological stressors and excess intake of caffeine can certainly be advocated, especially as many of these have been shown to be beneficial for primary prevention of CVD in their own right.

Both beta-blockade and I_f channel blockade with ivabradine can be recommended for the symptomatic relief of angina. Beta-blockers are recommended in patients who have had a myocardial infarction and, in carefully titrated doses, in heart failure. While I_f channel blockade may be an attractive choice in those intolerant of beta-blockade, its effects on prognosis, and therefore its independent therapeutic role, remain to be defined.

Blood Pressure

Blood Pressure Measurements

The large physiological variations in blood pressure mean that, to diagnose hypertension, blood pressure should be measured in each individual several times on several separate occasions. If systolic and/or diastolic blood pressure is only slightly elevated, repeated measurements should be made over a period of several months to achieve an acceptable definition of the individual's 'usual' blood pressure and to decide about initiating drug treatment. If systolic and/or diastolic blood pressure is more markedly elevated, repeated blood pressure measurements are required within a shorter period of time (weeks or days) in order to make treatment decisions. This is also the case if the blood pressure

elevation is accompanied by evidence of end-organ damage, associated clinical conditions, and/or by the concomitance of other cardiovascular risk factors that markedly increase overall cardiovascular risk. Repeated blood pressure measurements on several occasions are necessary to identify the relatively large number of persons in whom blood pressure elevation disappears following the first few visits. These individuals may need blood pressure measurements more frequently than the general population but drug treatment does not appear to be necessary because their cardiovascular risk is probably low.

Control of Arterial Hypertension

Table: Definition and Classification of Blood Pressure Levels

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120−129	and/or	80−84
High Normal	130−139	and/or	85−89
Grade 1 hypertension	140−159	and/or	90−99
Grade 2 hypertension	160−179	and/or	100−109
Grade 3 hypertension	≥180	and/or	≥110
Isolated systolic	≥140	and	<90

Isolated systolic hypertension should be graded (1, 2, 3) according to systolic BP values in the ranges indicated, provided that diastolic values are <90 mmHg. Grades 1, 2, and 3 correspond to classification of mild, moderate and severe hypertension, respectively. These terms have now been omitted to avoid confusion with quantification of total cardiovascular risk.

The decision to start pharmacological treatment, however, depends not only on the blood pressure level but also on total cardiovascular risk, which calls for a proper history, physical examination and laboratory examination to identify (i) the presence of clinically established cardiovascular or renal disease, (ii) the coexistence of other cardiovascular risk factors, and (iii) the presence of subclinical cardiovascular disease or end-organ damage. The presence of clinically established cardiovascular or renal disease (myocardial infarction, angina pectoris, heart failure, coronary revascularization, transient ischaemic attacks, stroke, renal insufficiency or overt proteinuria, peripheral arterial disease, advanced retinopathy, etc.) dramatically increases the risk of subsequent cardiovascular events regardless of the blood pressure level. This is also the case for the

association of hypertension and other cardiovascular risk factors such as diabetes (see table below).

Owing to the importance of target organ damage as an intermediate stage in the continuum of vascular disease and as a determinant of overall cardiovascular risk, signs of organ involvement should be looked for carefully.

Table: Factors Influencing Prognosis in Hypertension

Risk Factors	Target Organ Damage	Diabetes Mellitus	Established CV or Re Disease
• Systolic and diastolic BP levels	• Electrocardiographic LVH (Sokolow-Lyons >38 mm; Cornell >2440 mm × ms)	• Fasting plasma glucose ≥7.0 mmol/l (126 mg/dl)	• Cerebrovascular disease: ischaem stroke; cerebral haemorrhage; transient ischaer attack
		or:	
• Levels of pulse pressure (in the elderly)			
• Age (M >55 years; W >65 years)	or:	• Postload plasma glucose >11.0 mmol/l (198 mg/dl)	
• Smoking	• Echocardiographic LVH[a] (LVMI M ≥125 g/m^2, W ≥110 g/m^2		• Heart disease: myocardial infarction; angin coronary revascularizatior heart failure
• Dyslipidaemia			
• TC >5.0 mmol/l (190 mg/dl)	• Carotid wall thickening (IMI ≥0.9 mm) or plaque		
or			
• LDL-C >3.0 mmol/l (115	• Carotid-femoral pulse wave velocity >12 m/sec		

Risk Factors	Target Organ Damage	Diabetes Mellitus	Established CV or Re Disease
mg/dl) or • HDL-C: M <1.0 mmol/l (40 mg/dl), W <1.2 mmol/l (46 mg/dl) or • TG > 1.7 mmol/l (150 mg/dl) • Fasting plasma glucose 5.6−6.9 mmol/l (100-125 mg/dl) • Abnormal glucose tolerance test • Abdominal obesity (waist circumference >102 cm (M), 88 cm (W)) • Family history of premature CVD (M at age <55 years; W at age <65 years)	• Ankle/brachial BP index <0.9 • Slight increase in plasma creatinine M: 115-133 micromol/l (1.3-1.5 mg/dl) W: 107-124 micromol/l (1.2-1.4 mg/dl) • Low estimated glomerular filtration rate[b] (<60 ml/min/1.73 m^2) or creatinine clearance[c] (<60 ml/min) • Microalbuminuria 30-300 mg/24 h or albumin-creatinine ratio: ≥ 22 (M); or ≥31 (W) mg/g creatinine		• Renal disease: diabetic nephropathy; re impairment (serum creatinin M >133, W >124 micromol/l) proteinuria (>30 mg/24 h) • Peripheral artery disease • Advanced retinopathy: haemorrhages o exudates, papilloedema

Note: M, men; W, women; CV, cardiovascular disease; IMT, intima-media thickness; BP, blood pressure; TG, triglycerides; C, cholesterol. [a]Risk maximal for concentric LVH (left ventricular hypertrophy): increased LVMI (left ventricular mass index) with a wall thickness radius ratio ≥0.42. Modification of Diet in Renal Disease (MDRD) formula. [c]Cockcroft-Gault formula.

Who to Treat?

The decision to start antihypertensive treatment depends on systolic and diastolic blood pressure, as classified in the table above, and on total cardiovascular risk as estimated from the SCORE charts (see Figures 3-6 in the original guideline document). However, in hypertensive patients, prognosis is also affected by the presence or absence of target organ damage, diabetes mellitus, and established CV or renal disease (see table above).

Table: Management of Total CVD – Blood Pressure

In all cases, look for and manage all risk factors. Those with established CVD, diabetes or renal disease are at markedly increased and BP of <130/80 is desirable if feasible. For all other people, check SCORE risk. Those with target organ damage are managed as 'increased risk.'

SCORE CVD risk	Normal <135/85	High Normal 130−139/85−89	Grade 1 140−159/90−99	Grade 2 160−179/100−109	Grade 3 ≥180/110
Low <1%	Lifestyle advice	Lifestyle advice	Lifestyle advice	Drug Rx if persists	Drug Rx
Mod 1−4%	Lifestyle advice	Lifestyle advice	+ consider Drug Rx	Drug Rx if persists	Drug Rx
Increased 5−9%	Lifestyle advice	+ consider Drug Rx	Drug Rx	Drug Rx	Drug Rx
Markedly increased ≥10%	Lifestyle advice	+ consider Drug Rx	Drug Rx	Drug Rx	Drug Rx

Mod = moderate; Rx = treatment

How to Treat?

Lifestyle interventions include: weight reduction in overweight individuals; reduction in the use of sodium chloride to less than 3.8 g/day (sodium intake less than 1.5 g/day, i.e., 65 mmol/day); restriction of alcohol consumption to no more than 10 to 30 g/day ethanol in men (1-3 standard measures of spirits, 1-3 glasses of wine, or 1-3 bottles of beer) and to no more than 10 to 20 g/day ethanol in women (1 to 2 of these drinks/day); and regular physical activity in sedentary individuals.

Since tobacco smoking has a particularly adverse effect on the cardiovascular risk of hypertensive patients, intensive effort should be made to help hypertensive smokers to stop smoking.

As the blood pressure lowering effect of increased potassium has been well documented in the Dietary Approaches to Stop Hypertension (DASH) diet (rich in fruit, vegetables, and low-fat dairy products with a reduced content of dietary cholesterol as well as saturated and total fat), hypertensive individuals should be

generally advised to eat more fruits and vegetables (4 to 5 servings per day, i.e., 300 g) and to reduce intake of saturated fat and cholesterol.

Even in the absence of marked dyslipidaemia, hypertensive patients should be encouraged to change their diet in terms of fat content and composition.

Antihypertensive Drugs

The large number of randomized trials of antihypertensive therapy, both those comparing active treatment versus placebo and those comparing treatment regimens based on different compounds confirm that (i) the main benefits of antihypertensive treatment are due to lowering of blood pressure *per se*, and are largely independent of the drugs employed, and (ii) thiazide diuretics (chlorthalidone and indapamide), beta-blockers, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor antagonists can adequately lower blood pressure and significantly reduce cardiovascular morbidity and mortality. These drugs are thus all suitable for initiation and maintenance of antihypertensive treatment, either as monotherapy or in combination.

Identification of the first class of drugs to be used in the management of hypertension has always been a matter of debate. However, there is now conclusive evidence from trials that combination treatment is needed to control blood pressure in the majority of patients. Thus, if two or more drugs are likely to be required it is of marginal relevance which one is used in monotherapy for the first few weeks or months. However, drug classes (and even compounds within a given class) differ in type and frequency of adverse effects they may induce. Furthermore, drugs may have various effects on risk factors, target organ damage and hypertension-related events. When selecting an antihypertensive drug, the following should be taken into account: (i) the previous favourable or unfavourable experience of the individual patient with a given class of antihypertensive drugs (both in relation to blood pressure lowering and adverse events); (ii) the effect of drugs on cardiovascular risk factors in relation to the cardiovascular risk profile of the individual patient; (iii) the presence of target organ damage, associated clinical conditions, renal disease or diabetes, which may be treated more effectively by some drugs than by others; (iv) the presence of other coexisting disorders that may either favour or limit the use of particular classes of antihypertensive drugs; (v) the possibility of interactions with drugs used for other conditions present in the patient and (vi) the cost of drugs, either to the individual patient or to the healthcare provider. Cost considerations, however, should never predominate over efficacy, tolerability, and safety of the individual patient. Physicians should prefer drugs that have a long-lasting effect and a documented ability to effectively lower blood pressure over 24 hours with once-a-day administration. Simplification of treatment improves adherence to therapy, while effective 24-hour blood pressure control is prognostically important in addition to office blood pressure control. Long-acting drugs also minimize blood pressure variability and this may offer protection against progression of organ damage and risk of cardiovascular events.

Desirable Blood Pressure

The primary goal of treatment of the hypertensive patient is to achieve the maximum reduction in the long-term total risk of cardiovascular morbidity and

mortality. This requires treatment of all the reversible risk factors identified, including smoking, dyslipidaemia, or diabetes, and the appropriate management of associated clinical conditions, as well as treatment of the elevated blood pressure *per se*.

In all patients, however, the blood pressure reduction should be obtained gradually. This is particularly important in elderly patients, in those with isolated systolic hypertension, in patients with severe atherosclerotic disease, and in diabetic patients. In all these patients, an excessive orthostatic blood pressure value, which can be achieved, should be established by monitoring patients' symptoms, vital organ function, and well-being.

Blood Pressure Target in the General Hypertensive Population

On the basis of current evidence it can be recommended that in those who qualify for drug treatment, blood pressure be lowered at least to below 140/90 mmHg in all hypertensive patients and that lower values be pursued, if tolerated, in higher risk persons.

Duration of Treatment

Generally, antihypertensive therapy should be maintained indefinitely.

After prolonged good blood pressure control, it may be possible to attempt a careful progressive reduction in the dosage, or number of drugs, particularly in patients strictly following lifestyle recommendations. However attempts to step down treatments should be accompanied by careful, continued monitoring of blood pressure, particularly in high-risk patients and in patients with target organ damage. Careful consideration should be given to the fact that, in general clinical practice, hypertension is not well treated and that the number of patients in whom blood pressure is reduced to below 140/90 mmHg is a minority of the hypertensive population. Increasing adherence to antihypertensive treatment and achieving a wide blood pressure control in the population thus represents a major goal for clinical practice in the future.

Plasma Lipids

Exclusion of Secondary Dyslipidaemia

Hyperlipidaemias secondary to other conditions must be excluded before starting treatment, especially with drugs, since often the treatment of the underlying disease improves hyperlipidaemia and no other antilipaemic therapy is necessary. This is particularly true for hypothyroidism. Secondary hyperlipidaemias could be also caused by abuse of alcohol, diabetes, Cushing's syndrome, diseases of the liver and kidneys, obesity and several drugs (e.g., corticosteroids, isotretinoin and etretinate, cyclosporin). Patients who could have genetic dyslipidaemias such as familial hypercholesterolemia (FH) should, if possible, be referred to specialist evaluation, which might include molecular genetic diagnosis.

Diet

All patients with atherosclerotic disease, and persons at high risk of developing atherosclerotic disease, should follow the dietary recommendations given in chapter 8 of the original guideline document (see the section titled "Nutrition, Overweight and Obesity," above, in this summary). Some patients with severe hypertriglyceridaemia (>9 mmol/l) require a diet that is severely restricted in long-chain fatty acids from vegetable as well as animal sources and all patients with hypertriglyceridaemia should reduce alcohol intake. The purpose of this diet is to prevent pancreatitis. It differs substantially from the general dietary recommendations, and most patients will need the assistance of a well-trained dietician.

Physical Exercise

Patients with clinically established CVD as well as persons at high risk should follow the recommendations given in chapter 9 of the original guideline document (see the section titled "Physical Activity," above, in this summary). The major effect of physical exercise apart from a decrease in triglycerides is an increase in HDL-cholesterol.

Drugs

In most European countries, the current armamentarium of lipid-lowering drugs includes inhibitors of 3-hydroxy-3-methylglutaryl (HMG) coenzyme A (CoA) reductase (statins), fibrates, bile acid sequestrants (anion exchange resins), nicotinic acid and selective cholesterol absorption inhibitors such as ezetimibe. All of these drug classes, with the exception of cholesterol absorption inhibitors, have been shown in trials to reduce myocardial inflection and coronary death.

Drug Combinations: Effects and Side Effects

Lipid-lowering drugs can be used in combination and in some patients this is necessary to achieve the treatment goals both in familial hypercholesterolaemia and in combined hyperlipidaemia.

Lipid-Lowering Therapy in Acute Coronary Syndrome

Statins should be initiated while patients are in hospital with an acute coronary event.

Plasma lipids should be re-evaluated both at 4 to 6 weeks and 3 months after acute event and/or initiation of the lipid-lowering therapy to evaluate whether target levels have been achieved and to screen for liver dysfunction.

Goals of Therapy

It is still not clear what the ideal LDL-cholesterol value is, but there is evidence of benefit down to 2 mmol/l and even lower in all patients with established atherosclerotic disease.

Asymptomatic people at high risk of developing CVD, whose untreated values of total and LDL-cholesterol are already close to 5 (~190 mg/dl) and 3 mmol/l

(~115 mg/dl), respectively, will definitely benefit from further reduction of total cholesterol to less than 4.5 mmol/l (~175 mg/dl) and from further reduction of LDL-cholesterol to less than 2.5 mmol/l (~100 mg/dl) with lipid-lowering treatment.

However, these goals cannot be reached with the same ease by all patients. Patients with concentrations of plasma lipids that are only slightly abnormal can reach these goals of therapy fairly easily with diet and moderate doses of drugs. When these goals have not been reached in asymptomatic people at high risk they will still benefit to the extent that cholesterol has been lowered.

Should Statins Be Given to All Persons with CVD?

Relative risk reductions seem to be constant at all lipid levels, but absolute risk reductions are small in those with low lipid levels, with little evidence of a reduction in total mortality. The universal use of statins may be unrealistic in some economies.

A minority of patients have familial hypercholesterolemia or other severe, genetically determined disturbance of lipid metabolism. Even with dual or triple drug regimens, reducing LDL-cholesterol below 2 mmol/l (~ 80 mg/dl) can sometimes be difficult, and the physician must prepare the patient for that situation.

The current recommendations are that triglycerides greater than 1.7 mmol/l (~150 mg/dl) and HDL-cholesterol less than 1 mmol/l (~40 mg/dl) in men and less than 1.2 mmol/l (~45 mg/dl) in women continue to be regarded as markers of increased risk. However, triglycerides and HDL-cholesterol continue not to be regarded as goals of therapy. The main reason for this recommendation is that, in contrast to the evidence underpinning reduction of LDL-cholesterol, there is still not enough evidence from clinical trials defining to which levels triglycerides should be reduced, or HDL-cholesterol should be increased, to reduce risk of cardiovascular disease. Apart from being powerful indicators of risk, measurements of triglycerides and HDL-cholesterol should also be used to guide the choice of drug therapy as can non-HDL-cholesterol, for example, use of a drug with beneficial activity on these measures should be considered in patients where HDL-cholesterol and triglycerides are abnormal. The recommendations are summarized in Table 12 of the original guideline document.

Diabetes and Metabolic Syndrome

Treatment Targets in Patients with Type 2 Diabetes		
	Unit	**Target**
HbA_{1c} (Diabetes Control and Complications Trial [DCCT]-aligned)	HbA_{1c} (%)	≤6.5 if feasible
Plasma Glucose	Fasting/pre-prandial mmol/(mg/dl)	<6.0 (110) if feasible
	Post-prandial	<7.5 (135) if feasible

Treatment Targets in Patients with Type 2 Diabetes		
	Unit	**Target**
	mmol/l(mg/dl)	
Blood pressure	mmHg	≤130/80
Total cholesterol	mmol/l (mg/dl) mmol/l (mg/dl)	<4.5 (175) <4.0 (155) if feasible
LDL-cholesterol	mmol/l (mg/dl) mmol/l (mg/dl)	<2.5 (100) <2.0 (80) if feasible

The Metabolic Syndrome

1. The term 'metabolic syndrome' refers to the combination of several factors that tend to cluster together - central obesity, hypertension, low HDL-cholesterol, raised triglycerides and raised blood sugar – to increase risk of diabetes and CVD.
2. This implies that, if one component is identified, a systematic search for the others is indicated, together with an active approach to managing all of these risk factors.
3. Physical activity and weight control can radically reduce the risk of developing diabetes in those with the metabolic syndrome.

Risk of CVD, Coronary Heart Disease (CHD) and Stroke in Diabetes

Although a substantial proportion of the excess risk of atherosclerotic disease in both type 1 and type 2 diabetes is caused by the diabetic state itself and related factors, from the point of prevention of atherosclerotic disease it is important to emphasize that the conventional, modifiable major cardiovascular risk factors, elevated blood pressure, elevated LDL-cholesterol and smoking show in both type 1, and type 2 diabetic patients similar relationships with the risk of CVD as in nondiabetic patients. Because diabetes itself increases the absolute risk of cardiovascular disease, the additional impact of conventional risk factors leads to a more dramatic increase in absolute risk than in nondiabetic patients and thus the modification of these risk factors offers a great potential for prevention. Consequently, individualized global risk assessment and individualized prevention strategies are even more important in individuals with diabetes than in nondiabetic patients.

The Evidence for the Current Recommendations on Prevention of CVD in Diabetes

With the exception of glucose management, prevention of CVD follows the same general principles as for people without diabetes. A multifactorial approach to treatment and achieving low BP and low LDL are particularly important, thus many of the treatment targets are tougher for patients with diabetes.

Multifactorial Intervention

The typical type 2 diabetic patient suffers from many components of the metabolic syndrome, each of whom should be treated in accordance with existing guidelines.

In high risk patients polypharmacological multitargeted intervention is needed to obtain the maximal risk reduction.

Metabolic Syndrome

The majority of patients with type 2 diabetes have the risk factor characteristics of the metabolic syndrome and the presence of this risk factor clustering has an adverse effect on their prognosis. The diagnosis of the metabolic syndrome is, however, of greater importance in nondiabetic patients as an indicator of an increased risk of developing type 2 diabetes and CVD.

See the original guideline document for definitions of metabolic syndrome from the World Health Organization (WHO), National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and the International Diabetes Federation.

Management of Risk in Clinical Practice

Prevention of Diabetes

The optimal way to prevent the increased risk of CVD associated with diabetes would be through prevention of the disease in itself.

Glucose

In type 1 diabetes glucose control requires appropriate insulin therapy and concomitant professional dietary therapy. In type 2 diabetes professional dietary advice, reduction of overweight and increased physical activity should be the first treatments aiming at good glucose control. The impact of an effective lifestyle adjustment may be as effective as the prescription of an oral glucose-lowering agent.

Self-monitoring of blood glucose is essential in the treatment of type 1 diabetes to improve the safety and quality of treatment, and is a vital safeguard against serious hypoglycaemia. Self-monitoring may improve therapeutic efficacy and safety and should also be recommended for patients with type 2 diabetes.

There is a broad consensus between different guidelines on the glycaemic targets in type 1 diabetes. Insulin treatment, built upon appropriate nutrition and tailored on the basis of self-monitoring, which aims at Diabetes Control and Complications Trial (DCCT)-aligned HbA_{1c} targets, below 6.5%, has been recommended in patients who are at particularly high risk of CVD – those with clinically established CVD, microalbuminuria or nephropathy, history of early onset CVD and those with risk characteristics of the metabolic syndrome or other CVD risk factors. Age should also be taken into consideration in decisions on targets, because the risk of CVD begins to increase after the age of 35 years. Applying a lower target should

be accompanied by increasing caution regarding the avoidance of hypoglycaemic episodes.

In applying low targets to patients who receive treatment with insulin or drugs stimulating insulin secretion (sulphonylureas or rapid-acting insulin secretion-stimulating drugs, nateglinide or repaglinide) special attention should be paid to the avoidance of hypoglycaemic episodes with guidance obtained from glucose self-monitoring.

Blood Pressure

Targets for blood pressure are generally more ambitious in patients with diabetes.

The optimal BP levels to be achieved cannot be precisely defined, but values below 130/80 may be desirable in diabetic patients. In diabetic patients wish diabetic nephropathy and proteinuria >1 g/24 hr, values as low as 125/75 mmHg or lower are recommended if achievable without unacceptable side effects.

The type of antihypertensive medication also seems to be important. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor inhibitors have proven to be particularly effective in preventing progression from microalbuminuria to overt nephropathy in type 1 as well as in type 2 diabetic patients. Thus in these groups of patients, ACE inhibitors and angiotensin II receptor blockers would be preferred as initial therapy; however, most patients will require a combination of two or more drugs. Combination therapy including both an ACE inhibitor and an angiotensin II receptor antagonist has been shown to have additional beneficial effect, over and above the effect of each on progression of diabetic renal disease, and consequently this 'dual blockade' principle may be beneficial also in preventing CVD.

In diabetic patients with hypertension and established coronary heart disease particularly those who have survived a myocardial infarction and in those with angina pectoris, the use of beta-blockers is indicated.

Lipid-Lowering Therapy

In the absence of studies clearly defining treatment targets and in the presence of the excess risk in patients with diabetes, the treatment target in patients with diabetes should be: LDL-cholesterol less than 2.5 mmol/l (~100 mg/dl) and total cholesterol less than 4.5 mmol (~175 mg/dl) irrespective of the presence or absence of CHD or other atherosclerotic disease. But considering findings from some recent studies, particularly the Collaborative Atorvastatin Diabetes Study (CARDS) even lower targets [LDL-cholesterol <2.0 mmol/l (<80 mg/dl), total cholesterol <4.0 mmol/l (175 mg/dl)] may be applied, if feasible.

Based on trial experience on efficacy and safety of statins, these are currently recommended as the first choice for lipid-lowering drugs for people with type 1 and type 2 diabetes.

Antiplatelet Therapy

The use of aspirin or some other antiplatelet drug, if aspirin is contraindicated, may still be considered in the preventive management in diabetic patients who already have clinically established cardiovascular disease.

Precursors of Diabetes

Patients with impaired glucose tolerance (IGT) should be identified where possible and provided with necessary support.

Individuals with the metabolic syndrome are at high risk of developing cardiovascular disease, and in these individuals a total risk assessment based on the existing risk engines should be performed to assess risk, and to identify the most important risk factors available for intervention.

Prevention in Patients with the Metabolic Syndrome

The diagnosis of the metabolic syndrome is of greatest importance in nondiabetic patients as an indicator of an increased risk of developing type 2 diabetes and CVD. It is, however, important to emphasize that interest in the metabolic syndrome should not displace the use of conventional CVD risk assessment tools, such as SCORE and other similar risk scoring tools, from their primary place in the identification of individuals who are at high CVD risk. In fact, the components of the metabolic syndrome, with the exception of the measures of central obesity, triglycerides, impaired fasting glucose (IFG) and IGT, are included among the risk factor measurements used in conventional risk assessment systems. Adding waist circumference measurement to this set will give possibilities to detect the presence of the metabolic syndrome and help identify people who actually are at high risk of CVD, although they do not get particularly high risk scores in conventional CVD risk assessment. The original and revised National Cholesterol Education Program—Adult Treatment Panel III (NCEP-ATP III) definitions and the *International Diabetes Federation* (IDF) definition of the metabolic syndrome are suitable for clinical use, but it is important to realize that because of a lowered threshold for IFG in the revised NCEP-ATP III and IDF definitions and a lowered threshold for central obesity in the IDF definition, these definitions will pick up a larger proportion of people and will have a lower positive predictive value than the original NCEP-ATP III definition.

Since lifestyles have a strong influence on all the components of the metabolic syndrome, the main emphasis in the management of the risk in people with this syndrome should be in professionally supervised lifestyle change, particularly directed to the reduction of overweight and increased physical activity. Although the dyslipidaemia of the metabolic syndrome is characterized by elevated triglycerides and/or low HDL-cholesterol lipid management should, however, be steered with LDL-cholesterol goals in mind. Subgroup analyses of large statin trials have shown that coronary heart disease patients with and without the metabolic syndrome get from statin treatment a similar substantial relative reduction of CVD events, but the absolute benefit may be even greater in those with the syndrome, because they are at higher absolute risk.

Psychosocial Factors

Management of Psychosocial Risk Factors

Recommendations for the Management of Psychosocial Risk Factors In Clinical Practice

- Assess psychosocial risk factors, for example depression and hostility, low socio-economic status (SES), social isolation, and chronic life stress by clinical interview or standardized questionnaires.
- Discuss relevance with patient in respect to quality of life and medical outcome.
- Prescribe multimodal, behavioural intervention, integrating individual or group counselling for psychosocial risk factors and coping with stress and illness.
- Refer to a specialist in case of clinically significant emotional distress.

Recognizing the psychosocial risk associated with depression, hostility, low SES, lack of social support or chronic psychosocial stress in patients and persons with risk factors may be crucial as a means to reduce risk. Standardized measurements for depression, hostility, SES, social support or psychological stress are available in many languages and countries.

Alternatively, a preliminary assessment of psychosocial factors can be made within the physicians' clinical interview as detailed below.

Core Questions for the Assessment of Psychosocial Risk Factors in Clinical Practice

- Depression: Do you feel down, depressed and hopeless? Have you lost interest and pleasure in life?
- Social isolation: Are you living alone? Do you lack a close confidant? Do you lack any person to help you in case of illness?
- Work and family stress: Do you have enough control over how to meet the demands at work? Is your reward appropriate for your effort? Do you have serious problems with your spouse?
- Hostility: Do you frequently feel angry over little things? lf someone annoys you, do you regularly let your partner know? Do you often feel annoyed about habits other people have?
- Low SES: Do you have no more than mandatory education? Are you a manual worker?

For patients with low SES, lack of social support or chronic psychosocial stress, interventions need to focus on these areas in order to improve both their quality of life and medical outcome. lf available, patients should be recommended to join a multimodal, behavioural intervention that includes stress management and social reintegration. Whenever possible these interventions should occur on a group basis to enhance social interaction and improve social support. Depression and other negative effects tend to persist or even increase as cardiac disease progresses. While awaiting conclusive results that treating depression will alter CVD prognosis, a prudent approach at present is to offer patients with clinically significant depression treatment with psychotherapy and antidepressant medication, according to established guidelines. Those not accepting treatment should be closely followed and treatment offered again if depression persists for more than 4 to 6 weeks.

Inflammation Markers and Haemostatic Factors

Incorporation of C-reactive protein (CRP) and other emerging risk factors into routine practice for prediction of cardiovascular risk may be premature and criteria for the rigorous evaluation for such factors have been proposed. These criteria include: applicability to all relevant clinical cardiovascular events; ability to predict in short, intermediate and long-term follow-up; standardized measurements; examination of variability; the degree of correlation with established risk factors; and improvement in overall prediction, among other criteria.

Genetic Factors

Why Screen Close Relatives?

Close relatives of patients with premature CVD and persons who belong to families with inherited dysIipidaemias such as familial hypercholesterolaemia are at increased risk of developing CVD and should be examined for all cardiovascular risk factors.

Introduction

Genetic information may be divided into three categories: information on family history, information on phenotypes, and information on genotypes. All three types of information may be useful to identify patients who are at high inherited risk of developing CHD, and who may therefore warrant earlier or more aggressive therapeutic intervention to reduce modifiable risk factors (e.g., plasma cholesterol or blood pressure). Information on phenotypes and genotypes in combination may be particularly useful in guiding the particular therapeutic approach of choice.

Family History

Recommendations

Risk factor screening should be carried out in the first degree relatives of any patient developing coronary disease before 55 years in men and 65 years in women. A family history of premature CHD should also be taken into account in assessing the risk of developing the disease in a healthy individual, including the taking of detailed history and drawing of a pedigree. Lifestyle advice and, where appropriate, therapeutic management of risk factors should be offered to members of families where coronary disease is highly prevalent.

DNA-Based Test for Risk Prediction

In individuals in the general population, DNA-based tests do not, at the present time, add significantly to diagnostic utility or patient management, over-and-above the use of measures of established CHD risk factors. In the longer term, understanding disease aetiology in terms of genetic determinants may be useful in identifying high-risk individuals and adapting therapeutic management to the individual's genetic make-up.

Familial Hypercholesterolaemia (FH)

Because of their high CHD risk, patients with FH should be aggressively treated with statins at a young age, preferably in an experienced lipid clinic setting. Lifestyle advice should be offered and supported. Cascade testing to identify affected relatives should be undertaken. For optimal diagnostic and management results, both phenotypic and genotypic diagnosis may be considered.

Familial Combined Hyperlipidaemia (FCH)

Because of their high CHD risk, patients with FCH should be treated with lipid lowering therapy and lifestyle advice. There is currently little experience to support the clinical utility of cascade testing to identify affected relatives but this is likely to be beneficial.

Familial HDL Deficiency Syndromes

Once secondary causes have been ruled out, patients with a virtual absence of HDL must undergo careful physical examination for the clinical hallmarks of certain HDL deficiency syndromes. Family studies should be initiated, to demonstrate the vertical transmission of the low HDL cholesterol phenotype. Since currently there is no routinely-used drug available to increase HDL-cholesterol levels in patients with familial low HDL cholesterol, prevention of CVD in these patients should have the aim of the avoidance and treatment of additional risk factors.

New Imaging Methods to Detect Asymptomatic Individuals at High Risk for Cardiovascular Events

Unfortunately, sudden cardiac death is for many individuals the first manifestation of CVD. In others a large myocardial infarction or sever stroke may result in serious disability for the rest of their life. Therefore, one could think of a CVD detection programme as having the following objective: to identify those apparently healthy individuals who have asymptomatic arterial disease in order to slow the progression of atherosclerotic disease, to induce regression and in particular to reduce the risk of clinical manifestations.

The medical technology to detect atherosclerotic arterial disease is already available. However, during the last years an increasing number of modalities have been developed and, in some, their role in population screening has not yet been clearly evaluated.

Different criteria should be met including:

1. The noninvasive technique for detecting arterial disease is valid, precise, easy and acceptable.
2. The relationship between arterial disease detected noninvasively and the development of symptomatic CVD has been quantified.
3. There is a defined screening strategy and a defined intervention and follow-up policy.
4. Screening and intervention result in reduction of CVD events.
5. Screening has no adverse effects. (It should be noted that some of the imaging modalities may use pharmaceutical agents.)

For coronary artery disease, the consequences of coronary atherosclerosis can be objectively assessed noninvasively, using a variety of techniques such as bicycle or treadmill exercise ECG testing, stress echocardiography or radionuclide scintigraphy. These techniques are routinely used in diagnostic work-up programmes in the clinic; they have rarely been used in the population as screening tools. More recently, new techniques have become available to detect coronary lesions.

These new tests are based on the principle that atherosclerosis is a systemic disease of the arterial tree, with preferential involvement of the aorta and its large branches, coronary arteries, cerebral arteries, and lower-extremity arteries. Pathology studies have documented that levels of traditional risk factors are associated with the extent and severity of atherosclerosis. However, at every level of risk factor exposure, there is substantial variation in the amount of atherosclerosis. This variation in disease is probably due to genetic susceptibility combinations of different risk factors and interactions between genetic and environmental factors. Thus, measurements of subclinical disease, representing the current effect of risk exposures, may be useful for improving CHD risk prediction. Non-invasive tests such as carotid artery duplex scanning, electron beam computed tomography (EB-CT), multi-slice CT (MS-CT), ankle/brachial blood pressure ratios, and magnetic resonance imaging (MRI) techniques offer the potential for directly or indirectly measuring and monitoring atherosclerosis in asymptomatic persons.

Gender Issues: Cardiovascular Disease in Women

Despite the promise of observational epidemiology, hormone replacement therapy (HRT) has not been associated with a reduction in cardiovascular risk. In general, short-term HRT for symptomatic relief is not contraindicated but HRT is not currently advised for preventive purposes.

In general, women are disadvantaged at all stages of the evolution of CVD - risk is less often evaluated, chest pain is less likely to have a typical 'male' pattern (it has been suggested that the term 'atypical chest pain' may reflect the difficulty that male physicians have in listening to and understanding women), diagnostic tests are less likely to be performed and harder to interpret. In-hospital mortality for acute coronary syndromes is higher in women. Therapy may be delayed and mortality associated with interventions such as coronary artery bypass grafting has traditionally been reported to be higher, although this may no longer be the case.

Management implications:

1. European and national public health policy needs to address the problem of inadequate recognition of the size of the problem of CVD in women and to reflect this through publicity and education of both the public and the medical profession.
2. Clinicians likewise need vigilance in understanding the need to think risk and CVD in dealing with female patients.
3. The principles of total risk estimation and management are the same for both sexes, with particular emphasis on the evaluation of smoking, weight, the use of oral contraceptives and glucose tolerance in women.

4. The fact that a low absolute risk may conceal a high relative risk which, if managed effectively, need not translate into a high absolute risk in later life. In this situation, detailed help with lifestyle change is in general more important that drug treatment.

Renal Impairment as a Risk Factor in Cardiovascular Disease

Renal Impairment and Cardiovascular Risk

1. Risk of CVD rises progressively from microalbuminuria with preserved glomerular filtration rate (GFR) to end stage renal disease when it is 20 to 30 times that of general population.
2. Applies to apparently healthy people and to those with hypertension, CVD and heart failure.
3. Associated with high blood pressure, hyperlipidaemia, metabolic syndrome, uric acid, homocysteine, anaemia.
4. Particularly vigorous risk factor control needed.

Cardioprotective Drug Therapy

When to Prescribe Cardioprotective Drugs in Addition to Those Used to Treat Blood Pressure, Lipids and Diabetes?

1. Aspirin for virtually all with established CVD, and in persons at >10% SCORE risk once blood pressure has been controlled.
2. Beta-blockers after myocardial infarction and, in carefully titrated doses, in those with heart failure.
3. ACE inhibitors in those with left ventricular dysfunction and in diabetic subjects with hypertension or nephropathy.
4. Anticoagulants in those at increased risk of thromboembolic events, particularly atrial fibrillation.

In addition to drugs to control symptoms, manage blood pressure, lipids and glucose levels to goal, the use or prophylactic drugs shown in clinical trials to reduce CVD morbidity and mortality must be considered. While some of these drugs are appropriate for all individuals at high total risk, whether from established CVD or at high risk of developing CVD, others are specifically indicated for selected patients.

Antiplatelet Therapies

Patients with Atherosclerotic Disease

Aspirin or other platelet modifying drugs are recommended in all patients at high risk of occlusive arterial disease unless there are specific contraindications.

Clopidogrel together with aspirin is indicated in all patients suffering from an acute coronary event (unstable angina (UAP), non-ST-segment myocardial infarction

[NSTEMI], ST-segment myocardial infarction [STEMI]) for a period of 9-12 months. In chronic atherosclerotic disease, clopidogrel should only be considered as an alternative to aspirin in the case of aspirin allergy.

In Patients with Diabetes Mellitus

At present aspirin use is recommended only in those with established CVD.

Asymptomatic High Risk Individuals

In asymptomatic individuals with no evidence of cardiovascular disease a meta-analysis has shown that aspirin reduced the risk of the combined end point of nonfatal myocardial infarction and fatal CHD, but increased the risk of haemorrhagic strokes and major gastrointestinal bleeding. The net benefit of aspirin increased with increasing cardiovascular risk and therefore estimating total risk of CVD is an absolute prerequisite to initiating antiplatelet therapy. If the total CVD risk is >10% over 10 years then prophylactic aspirin is appropriate as long as the blood pressure has been controlled as closely as possible to the goal of less than 140/90 mmHg. In lower risk individuals in the population a small absolute vascular benefit by aspirin may be offset by the slightly greater absolute risk of bleeding complications. When aspirin cannot be tolerated alternative antiplatelet therapy such as clopidogrel should be considered.

Therefore aspirin (75 mg daily) can be considered in all patients with CVD, and those at high risk of developing CVD (SCORE > 10% over 10 years) once the blood pressure has been controlled.

Beta-blockers

Beta-blockers are indicated, providing there are no contraindications, (i) in the treatment of heart failure, (ii) as prophylaxis following myocardial infarction, including patients with diabetes; (iii) to relieve symptoms of myocardial ischaemia; and (iv) to lower blood pressure to the goal of less than 140/90 mmHg, except in diabetic patients where alternative classes of antihypertensive drugs can be considered before beta-blockers.

ACE Inhibitors

Cardiovascular Disease

ACE inhibitors are indicated in all patients, unless there are contraindications, for the following reasons: (i) treatment of left ventricular dysfunction with or without over heart failure; and (ii) to reduce blood pressure to goal less than 140/90 mmHg.

Patients with Diabetes Mellitus

ACE inhibitors are indicated in patients with diabetes mellitus, unless there are contraindications, for the following reasons: (i) to reduce blood pressure to goal less than 130/80 mmHg, and (ii) type 1 and (possibly) type 2 diabetic nephropathy.

Asymptomatic High Risk Individuals

ACE inhibitors are indicated in asymptomatic high risk patients, unless there are contraindications, for the reason of reducing blood pressure to goal less than 140/90 mmHg.

Angiotensin-Receptor Blockers (ARBs)

Generally speaking ARBs are indicated in all patients who have an indication for ACE inhibitor therapy, but cannot tolerate ACE-inhibitors, for example, due to side effects. In addition, ARBs in combination with ACE inhibitors can reduce morbidity (i.e., rate of rehospitalization) in patients suffering from congestive heart failure.

Calcium Channel Blockers (CCBs)

This drug class has been shown to reduce cardiovascular outcomes in people with arterial hypertension.

In post-MI patients with contraindications to beta-blockers and no evidence of heart failure, verapamil may be considered based on the results of a single large clinical trial.

Calcium channel blockers are indicated for the reason of reducing blood pressure to target less than 140/90 mmHg or less than 130/80 mmHg (diabetes).

Diuretics

Diuretics are indicated for the following reason: to reduce blood pressure to target less than 140/90 mmHg. Thiazide diuretics are not recommended as first-line antihypertensive agents in diabetic patients or those at high risk of developing type 2 diabetes.

Anticoagulation

Systemic anticoagulation with coumarins is generally not indicated prophylactically in patients with coronary artery disease. However anticoagulation can be considered in selected patient following myocardial infarction at increased risk of thrombo-embolic events including patients with large anterior myocardial infarction, left ventricular aneurysms or thrombus, paroxysmal tachyarrhythmias and chronic heart failure, particularly in combination with aspirin. In patients with paroxysmal or permanent atrial fibrillation, systemic anticoagulation is indicated as shown in the table below.

In patients with coronary heart disease (CHD) or other cardiac disease, systemic anticoagulation is indicated for the following reasons:

i. History of thrombo-embolic events
ii. Left ventricular thrombus

Table: Indications for Antithrombotic Therapy in Patients with Atrial Fibrillation

Risk Category	Recommended Therapy
No risk factors	Aspirin, 81 to 325 mg daily
One moderate-risk factor	Aspirin, 81 to 325 mg daily, or warfarin (INR 2.0 to 3.0, target 2.5)
Any high-risk factor or more than 1 moderate-risk factor	Warfarin (INR 2.0 to 3.0, target 2.5)[a]

Less Validated or Weaker Risk Factors	Moderate-Risk Factors	High-Risk Factors
Female gender	Age greater than or equal to 75 years	Previous stroke, TIA or embolism
Age 65 to 74 years	Hypertension	Mitral stenosis
Coronary artery disease	Heart failure	Prosthetic heart valve[a]
Thyrotoxicosis	LV ejection fraction 35% or less Diabetes mellitus	

INR, international normalized ratio; LV, left ventricular; TIA, transient ischaemic attack. [a]If mechanical valve, target international normalized ration (INR) greater than 2.5

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Assessing total cardiovascular disease (CVD) risk
- Smoking cessation
- Management of total CVD risk - lipids

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Reduction in the incidence of first or recurrent clinical events due to coronary heart disease, ischaemic stroke, and peripheral artery disease

- Prevention of disability and early death
- Prevention of clinical cardiovascular disease

POTENTIAL HARMS

Side effects of recommended medications are discussed in the original guideline document in the context of compliance and limitations of use.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Beta-blocker-thiazide combinations have been associated with metabolic disturbance and new-onset diabetes and may have specific contraindications in patients prone to diabetes.
- Angiotensin-converting enzyme (ACE) inhibitors are indicated in all patients, unless there are contraindications for the following reasons; (i) treatment of left ventricular dysfunction with or without overt heart failure; and (ii) to reduce blood pressure to goal less than 140/90 mmHg.
- Angiotensin-converting enzyme (ACE) inhibitors are indicated in all patients with diabetes mellitus unless there are contraindications for the following reasons: (i) to reduce blood pressure to a goal less than 130/80 mmHg, and (ii) type 1 and (possibly) type 2 nephropathy.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The European Society of Cardiology (ESC) Guidelines represent the views of the ESC and were arrived at after careful consideration of the available evidence at the time they were written. Health professionals are encouraged to take them fully into account when exercising their clinical judgement. The guidelines do not, however, over-ride the individual responsibility of health professionals to make appropriate decisions in the circumstance of the individual patients in consultation with that patient, and, where appropriate and necessary, the patient's guardian or carer. It is also the health professional's responsibility to verify the rules and regulations applicable to drugs and devices at the time of prescription.
- At the outset, it is stressed that these guidelines are just that, and not didactic rules. They should be interpreted in the light of the clinician's own knowledge and judgement, the patient's view, and in the light of local conditions and practicalities and as new knowledge becomes available. Indeed the development of national guidelines is strongly encouraged with objectives priorities and implementation strategies that are adapted to suit local conditions both medical and economic.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

What would make the practice of cardiovascular disease (CVD) prevention easier?

1. Simple, clear, credible guidelines
2. Sufficient time
3. Positively helpful government policies (defined prevention strategy with resources, incentives including remuneration for prevention as well as treatment)
4. Educational policies that facilitate patient adherence to advice

Barriers to the Implementation of Guidelines

It is essential that clinical guidelines are in concordance with priorities in the health system and with ethical values most clinicians can agree upon. If not, this may be an important reason why many clinicians do not follow guidelines.

The implementation of these guidelines should be based on national surveys to adjust them to the stratification of risk factors and premature CVD death in the individual country and bring them in accordance with priorities set by the health authorities and the professional bodies. The workload put on the health system should be affordable and should not imply that resources should be allocated to prevention strategies when the outcome for the population is better by alternative use.

Given agreement that the implementation of prevention is a priority, the next step in the implementation of these guidelines is the involvement of the clinicians in primary and secondary care.

Analyses of the barriers to changing practice, such as a review of 76 doctors, have shown that obstacles to change in practice can arise at different stages in the healthcare organization, or the wider environment. Most theories on implementation of evidence in healthcare emphasize the importance of developing a good understanding of such obstacles to develop an effective intervention (see Table 21 in the original guideline document).

Doctor-Patient Relationship

The preventive interventions must be based on a patient-centered approach, where the doctor pays full attention to appraise and meet the patient's concerns, beliefs and values, and respects the patient's choice even if it is not in concordance with the doctor's first proposal. The changing of lifestyle or taking medication often means for the rest of the patient's life, so the decision must be owned by the patient. Therefore, treatment goals should be set in collaboration with the patient, taking into account the values and priorities of the patient. If the treatment goals are unaffordable, it may lead to frustration and clinical neglect, by the doctor and the patient. The doctor should explore the patient's important values, beliefs and expectations regarding the prevention measures to be taken.

Physician-Related Methods to Improve Implementation

It has been argued that the application of guidelines in a setting of rigorous control gives the best chances to improve clinical practice. However most front-

line clinicians work in settings where such control is not practical, and mostly not wanted. The very character of this specific task – primary and secondary prevention – is not suitable for this strategy.

Audit and feedback, where practitioners are given data on their performance, is another tool that has been used to improve practice. It seems logical that practitioners will change their practice when they get feedback indicating that their present practice is inconsistent with that of their peers or with evidence based guidelines. A recent meta-analysis from the Cochrane collaboration shows that the effect of audit and feedbacks, if any, is modest.

The decision to start preventive measures and follow them up is more value-related than treatment of established disease, so the values and attitudes of the doctors and the patients are more important. In addition, most clinical decisions are taken more intuitively, on the basis of recognition patterns or other internal mental shortcuts (heuristics) of the individual doctor. How this affects the application of guidelines is not known, and more research is needed.

Important Arenas for Training

There is a need for training of doctors in patient-centered preventative care, with emphasis on:

- Patient-centered methods in the consultation process
- The motivation to change – how to support and strengthen the patient's decision for healthy habits
- How to evaluate multifactorial risk and use risk charts
- How to communicate risk and the effects of interventions
- How to discuss treatment goals and follow up

Implementation Strategies

1. On the European (international) level:
    a. Publication of the guidelines in relevant journals.
    b. Presentation at International conferences arranged by the participating societies.
    c. Involvement in policy at European Union level through, for example, the Luxembourg Declaration and the development of the European Heart Health Charter.
2. On the national level:

    a. If not already existing, the implementation demands a leading expert group of national organizations representing similar groups as the European Task Force. The group should have acceptance and support from national health authorities.
    b. Adjustment and application of national standards in accordance with the European Guidelines.
    c. Further implementation should be organized by the National Colleges in accordance with the local needs, see below.

The implementation strategies should consist of a package of different measures working in combination:

1. A public stealth approach, with emphasis on smoking cessation, healthier food and better access to physical activity in all ages should be implemented – to support and complement the individual-oriented high risk strategy of doctor-initiated prevention.
2. A public information campaign of the Joint CVD Prevention Guidelines with 2 main topics:
    a. Information of the concept of multiple risk assessment and treatment and the intervention thresholds.
    b. What people can do to reduce the risk. The message should encourage people with high risk to realise their risk and go to see a doctor, but should reassure people with low risk that they can stay healthy without the doctor's help.
3. An information and education program aimed at practicing doctors (general practitioner [GPs], internists, other). It should consist of a selection of the effective strategies mentioned above:

    a. Lectures and CME activities with interactive participation.
    b. Audit and feedbacks preferably combined with outreach visits by trained colleagues.
    c. Dissemination of electronic versions, applicable for handheld equipment.
    d. Dissemination of simple one sheet versions of risk algorithms and treatment recommendations.

IMPLEMENTATION TOOLS

Clinical Algorithm
Personal Digital Assistant (PDA) Downloads
Pocket Guide/Reference Cards
Slide Presentation
Staff Training/Competency Material

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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GUIDELINE COMMITTEE

Task Force of European Society of Cardiology and other Societies on Cardiovascular Disease Prevention in Clinical Practice

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Czech Society of Cardiology - Medical Specialty Society
Estonian Society of Cardiology - Medical Specialty Society
Finnish Cardiac Society - Medical Specialty Society
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Swiss Society of Cardiology - Medical Specialty Society
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This is the current release of the guideline.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.

Print copies: Available from Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK, Tel: +44 (0) 1865 353263, Fax: +44 (0) 1865 353774, Web site: http://www.eurheartj.oxfordjournals.org/.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- European guidelines on cardiovascular disease prevention in clinical practice. Executive summary. Available in Portable Document Format (PDF) from the European Society of Cardiology (ESC) Web site.
- European guidelines on cardiovascular disease prevention in clinical practice. Slide set. 2007 Sep. Available in Portable Document Format (PDF) from the ESC Web site.
- Cardiovascular disease prevention. Pocket guidelines. Order form available in Portable Document Format (PDF) from the ESC Web site. Also available for PDA download from the ESC Web site.

Print copies: Available from Oxford University Press, Great Clarendon Street, Oxford, OX2 6DP, UK, Tel: +44 (0) 1865 353263, Fax: +44 (0) 1865 353774, Web site: http://www.eurheartj.oxfordjournals.org/.

Additionally, continuing medical education (CME) credit is available online at the European Society of Cardiology (ESC) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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